

**1,6-Hexamethylene bis(3,5-di-(tert)-butyl-4-hydroxyhydrocinnamate -
Comments of Environmental Defense**

(Submitted via Internet 10/22/02)

Environmental Defense appreciates this opportunity to submit comments on the robust summary/test plan for 1,6-Hexamethylene bis(3,5-di-(tert)-butyl-4-hydroxyhydrocinnamate.

The Robust Summary/Test Plan for 1,6-Hexamethylene bis (3,5-di-(tert)-butyl-4-hydroxyhydrocinnamate) (Irganox 259), submitted by Ciba Specialty Chemical Corporation, indicates this chemical is used almost exclusively as an antioxidant in the polymer industry. As such, its use is limited to industrial applications. Occupational exposure is said to be low. Exposure of the public and the environment is further limited by the facts that (i) Irganox 259 is incorporated into the polymeric products in which it is used and (ii) its very low water solubility limits its migration from these products. Concern regarding possible adverse effects on the public and/or the environment resulting from an accidental release of this compound is raised by the fact that Irganox 259 is not readily biodegradable. However, this concern is lessened by the fact that the very low water solubility of this compound results in a prediction that Irganox 259 released into the environment will partition almost exclusively into soil and sediment. Concern regarding environmental or human exposure is also lessened by the fact that a number of studies indicate Irganox 259 has very low toxicity and is neither mutagenic nor carcinogenic. Low reproductive and developmental toxicity are predicted by the results of several repeat-dose studies that indicate a lack of effect on the male and female reproductive organs.

However, occupational exposures could be of concern with regard to effects on the thyroid, which toxicology studies indicate is one of the most sensitive target tissues of exposed animals. Although we do not know the mechanism involved, we speculate this toxicity may result from metabolism of Irganox 259 to free cinnamic acid that may act interfere with the synthesis of L-tyrosine, the precursor of thyroxine. Given the very low solubility of Irganox 259, it is likely that most of the high doses administered in the toxicity studies were never absorbed from the gastrointestinal tract. If that is the case, the toxicity of this compound at low levels of Irganox 259 encountered in occupational exposures would be underestimated by the results of animal studies. Thus, although we do not anticipate release of this compound into the environment or exposure of the general public to result in adverse effects, producers and users of Irganox 259 should closely monitor their workers for adverse effects on thyroxine levels and thyroid function.

In summary, the Robust Summary for Irganox 259 is complete and well organized. Available data are sufficient to address the requested SIDS elements and are summarized in a concise Test Plan. The Test Plan clearly describes the uses, available studies and presents the data in is carefully organized tables. (One minor formatting note: The first seven pages of the Test Plan are presented again virtually verbatim in the subsequent pages, and the pagination of the pages after these first seven pages is unusual. That is, after the first seven pages of the Test Plan and throughout the Robust Summary the pages are numbered 2 of 2, 3 of 3, 4 of 4, etc., to 54 of 54.)

Thank you for this opportunity to comment.

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